REMARKS

Claims 13-27 are pending in this application. The Applicants have amended claim 26 and have cancelled claims 13-25, without prejudice or disclaimer. Claims 28-39 have been added.

Upon entry of the present amendment, claims 25-39 are pending in this application.

I. Election Restriction

Applicants have amended the claims without prejudice or disclaimer, to embrace the subject matter of elected Group I. All non-elected subject matter has been cancelled, without prejudice or disclaimer, to be filed in a subsequent divisional application.

II. Rejection under 35 U.S.C. § 112, first paragraph

The Office has rejected claims 13-27 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the diseases/conditions selected from inflammation, rheumatoid arthritis, pain, common cold, osteoarthritis, etc., allegedly does not provide enablement for all of the diseases/conditions mediated by prostaglandin such as those found in claim 26. The Office alleges that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

At the outset, the Applicants acknowledge and appreciate the Examiner's indication that the diseases/conditions selected from inflammation, rheumatoid arthritis, pain, common cold, osteoarthritis, etc., are enabled by the specification. As such, the Applicants respectfully submit that the following diseases/conditions are enabled by the specification: pain, fever or inflammation associated with rheumatic fever, influenza or other viral infections, common cold, low back and neck pain, skeletal pain, post-partum pain, dysmenorrhea, headache, migraine, toothache, sprains and strains, myositis, neuralgia fibromyalgia synovitis arthritis, including rheumatoid arthritis, degenerative joint diseases (osteoarthritis), gout and ankylosing spondylitis, bursitis, burns including radiation and corrosive chemical injuries, sunburns, pain following surgical and dental procedures, bone fracture, and presurgery.

The Applicants respectfully contend that claims 26-39 are enabling with respect to the full scope of the claims; however, in order to advance the prosecution of the present invention, the Applicants have amended claim 26. The Applicants preserve their right to file a divisional application directed to the cancelled subject matter in due course.

Upon review and consideration of the Office's rejection, the Applicants contend that the specification enables any person skilled in the art to which the invention pertains, or with which it is most nearly connected, to use the invention commensurate in scope with amended claim 26.

The Applicants respectfully submit that one skilled in the art would find the asserted utility of the claimed compounds consistent with knowledge in the art at the time of the filing of the present invention. The scientific literature establishes a direct relationship between prostaglandin EP4 receptor antagonists and the claimed utilities. To establish this relationship, the following literature references are provided in Table I, below, which describe the link between the mechanism of the claimed compounds and the claimed utilities.

Table I

Claimed Disorder	**Literature Reference**	**Disorder in Literature Reference**
immune and autoimmune diseases; allergic rhinitis, atopic dermatitis, asthma or eosinophil related disorders	US03-0236260A1	Taken together, the references discuss the use of EP4 receptor ligands in the treatment of IL-6 involved diseases. The role of IL-6 in autoimmune disease (eg rheumatoid arthritis) and the regulation of IL-6 production by EP4 are addressed specifically.
	Therapy of rheumatoid arthritis by blocking IL-6 signal transduction with a humanized anti-IL-6 receptor antibody, Yoshizaki et al., Springer Semin Immunopathol. Vol. 20, 247 259, 1998.	
	The role of macrophages in atherogenesis, Libby et al., Curr. Opin. Lipidol. Vol. 4, 355-363 (1993).	

	Binary regulation of interleukin (IL)-6 production by EP_1 and EP_2/EP_4 subtypes of PGE_2 receptors in IL-1 β-stimulated human gingival fibroblasts, Noguchi, K., et al., J. Periodont Res, Vol. 37, 29-36 (2002).	
cellular neoplastic transformations or metastic tumor growth	Involvement of Prostaglandin E Receptor Subtype EP_4 in Colon Carcinogenesis, Mutoh, M., et al, Cancer Research, Vol. 62, 28-32, (2002).	States that EP_1 and EP_4 antagonists may be good candidates as chemopreventive agents against colon cancer and provides data suggesting that PGE_2 mediates colonic carcinogenic changes by acting at EP_1 and EP_4 receptors in the colon
Alzheimer's disease	Expression of Interleukin-6 in Atherosclerotic Lesions of Male ApoE-Knockout Mice. American Heart association 1498-1505, (1998)	Increased levels of interleukin-6 have been proposed to contribute to a number of pathological disorders, including osteoporosis and Alzheimer's disease.
Sleep disorders	Prostaglandin E (EP) receptor subtypes and sleep: promotion by EP_4 and inhibition by EP_1/EP_2, Yoshida, Y, et al, Neurophysiology, Vol. 11, 2127-2131 (2000).	Results indicate that the sleep-promoting effect prostaglandin E receptor subtypes is brought about mainly through activation of EP_4 receptors
bone loss; osteoporosis; promotion of bone formation	Impaired Bone Resorption to Prostaglandin E_2 in Prostaglandine E Receptor EP4-knockout Mice, Miyaura, C., et al., J. Biological Chemistry, Vol. 275, 19819-19823 (2000).	Findings suggest that PGE_2 stimulates bone resorption by a cAMP-dependent mechanism via the EP4 receptor; study also suggests that specific antagonists for EP4 may be useful in regulating PGE-mediated metabolic bone diseases
	Effect of Selective Prostaglandin EP4 Receptor Antagonist on Osteoclast Formation and Bone Resorption In Vitro, Tomita, M., et al., Bone, Vol. 30, 159-163 (2002).	results of EP4 receptor agonist study may point to a new approach for the therapy of bone loss, not only in inflammatory disorders but possibly also in osteoporosis

	Stimulation of bone formation and prevention of bone loss by prostaglandin E EP4 receptor activation, Yoshida, K., et al, PNAS, Vol. 99, 4580-4585 (2002).	Provides results suggesting that activation of EP4 induces bone remodeling *in vivo* and that EP4-selective drugs may be beneficial humans with osteoporosis; study suggests that EP4 activation stimulates *de novo* bone formation
Kidney disease	Differential regulation of renal prostaglandin receptor mRNAs by dietary salt intake in the rat, Jensen, B, et al., Kidney International, Vol. 56, 528-537, (1999).	Results suggest a region-specific regulation of PGE2 EP3 and EP4 receptor expression by dietary salt intake in the rat kidney.

The Applicants respectfully contend that literature references provided above, together with the other literature cited in the application, provide guidance to one of skill in the art for a link between the prostaglandin EP4 receptor antagonists of the present invention and the claimed diseases/disorders.

As a courtesy to the Examiner, copies of the literature references discussed above are attached hereto.

Accordingly, the Applicants respectfully submit that the rejection of claims 13-27 (now claims 26-39) under 35 U.S.C. §112, first paragraph, has been overcome by the present amendment. The Applicants respectfully request that the rejection be withdrawn.

III. Double Patenting

The office has rejected claims 13-27 under the judicially created doctrine of obviousness-type double patenting. Applicants respectfully submit that upon notification of allowance of the presently pending claims, that Applicants will timely file a Terminal Disclaimer.

IV. Conclusion

Upon entry of the present amendments, the Applicant submits that this application is now in condition for allowance, which allowance is respectfully solicited.

If the Examiner believes that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at 734-622-7304.

In view of the present amendment and foregoing remarks, reconsideration of the objection and advancement of the case to issue are respectfully requested.

The Commissioner is authorized to charge any fee or credit any over payment in connection with this communication to our Deposit Account No. 23-0455.

Respectfully submitted,

Dated: 4/26/05

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